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DYSPNEA

In the early days of modern physiology the emphasis in respiratory control in health and disease was placed on reflexes and clinical dyspnea was held to be due to afferent nerve impulses from the lungs.[8] Subsequent developments led to the concentration of attention on the effects of chemical agents directly on the respiratory center and any increase in breathing came to be regarded as the result of an increase in the effective chemical stimulation of the center; if no increase in the chemical stimulus could be detected this was assumed to be because existing methods were too crude for the purpose, because the chemical stimulant was something else, because it was in higher concentration in the center than in the arterial blood, or because the center had somehow become more sensitive to it.[2, 3, 5] During the past two decades, however, a series of events has brought the attention of physiologists back to the reflex factor in respiratory control and as a result it has become evident that the hyperpneas associated with induced emergencies such as anoxemia, acidosis and muscular exercise[2, 5, 7] as well as many, if not most, clinical dyspneas[1, 5] are due to afferent nerve impulses, not to the direct action of chemical agents on the respiratory center. The reflexes concerned are now known to be much more numerous and their interrelationships more complex than had previously been suspected, and the only dogmatic statements that can now be made about dyspnea in health or disease are that it may be due to a number of factors which vary according to the condition, that it is practically never dependent on a single factor, and that it is not susceptible to a single, all-inclusive explanation.

		Stimulant Reflexes From				Impulses from Cortex	Increased Temperature	Direct stim. of center by	
		Lungs	Chemo-receptors	Presso-receptors	Elsewhere			↑pCO_2	↑cH
Physiological	CO_2 inhalation		±					++++	+?
	Acid ingestion		++					++	+?
	Anoxemia		++++			+?			
	Asphyxia		++++			+?		++++	+?
	Exercise		+		++	+	++	±	+?
Heart disease		++++	+			+?		+?	+?
Pneumonia		++	++++		+		++	±	
Atelectasis		++++	++					±	+?
Emphysema		++	++					+	+?
Pulmonary embolism		++++	++++					±	+?
Asthma		++	+					±	+?
Anemia					+?			+?	+?
Shock Hemorrhage, etc.				++		+?		+?	+?
Ether anesthesia		++			+				

In the above table we have summarized the data now available on the cause of the dyspnea encountered in five physiological and eight pathological states in which dyspnea characteristically occurs, and have also included one (ether anesthesia) in which breathing, while not dyspneic, is not depressed as it is by other anesthetic agents. Each vertical column deals with one influence that has been proved capable of stimulating respiration, either through nerve impulses to the center or by direct action upon it. Some of these may be new to clinicians, and others now occupy places quite different from those assigned to them even ten years ago. A brief explanation of the meaning of each therefore seems desirable.

Under "Stimulant Reflexes from the Lungs" we include all respiratory stimulant afferent impulses carried by the vagus nerves except those from the aortic arch and aortic body (or bodies). Impulses aroused by distention and collapse of the air ducts and spaces (Hering-Breuer reflexes) are included here, as well as any others that may be set up in pulmonary tissues by irritation, congestion, secretions, exudates or foreign agents. By "Chemoreceptors" we mean the chemically sensitive nerve structures in the carotid and aortic bodies; these are now known to be responsible for the dyspnea of anoxemia and of certain drugs and poisons such as cyanides, sulfides, lobeline, nicotine, etc. and for part (perhaps all) of the air-hunger of advanced acidosis[5, 7]; they are also suspected of playing a part in the hyperpnea of fever[5]. The "Pressoreceptors" are the pressure-sensitive nerve endings in the carotid sinus and aortic arch regions; these are more important to circulatory control than to respiratory but under special circumstances they may contribute to dyspnea[5]. "Impulses from Cortex" provides for hyperpnea from impulses originating in parts of the neuraxis above the medulla, such as impulses resulting from fear, anxiety or other psychic factors, and particularly for those from the motor cortex during voluntary muscular efforts[2, 3]. "Increased Temperature" is given a special column because existing information does not permit decision as to whether fever stimulates breathing directly or reflexly[2, 5]. The last two columns provide for stimula-

tion of the respiratory center by the direct action of chemical stimuli upon it. "| pCO_2" means that the CO_2 tension existing in the center has increased, either because of a rise in the CO_2 tension in the arterial blood or because the blood supply of the center has been reduced to the point at which products of the center's own metabolism can no longer be carried away as fast as they are formed. By "| cH" we mean increased hydrogen ion concentration in the center; this column is included because this factor has long dominated discussions of respiratory control although recent evidence[2, 5] indicates that the center is relatively insensitive to the hydrogen ion.

The number of + signs is intended to show the importance of this factor in this condition, relative to the other conditions listed. The ± symbol indicates that this agency may or may not be brought into action; if it is, it plays a part in the final dyspnea but the latter can occur about as well without it. The ? mark signifies uncertainty as to the presence or assigned importance of this factor in this condition.

A glance at the table shows that, according to information now available, there is no single, all-inclusive explanation for dyspnea. The long-dominant explanation—increase in the chemical stimulus acting on the center—is applicable only in the cases of CO_2 inhalation and asphyxia, in both of which CO_2 retention occurs for obvious reasons. In acidosis there may be a temporary rise in arterial CO_2 tension because of reduction in the alkali reserve, but in clinical acidosis breathing evidently is stimulated by something else because CO_2 tension often is subnormal[6]; reflexes from the chemoreceptors are probably responsible for this and there is reason to suspect that the carotid and aortic bodies may be the only parts of the respiratory regulating system that are directly stimulated by the hydrogen ion[5, 7]. In anoxemia the hyperpnea is now known to depend largely, perhaps wholly, on reflexes from the chemoreceptors[5, 7]; the alkalosis and fall in arterial CO_2 tension associated with anoxemia are due to the fact that these reflexes have become the dominant element in respiratory control and the normal chemical stimulus (CO_2) is reduced accordingly—a consideration that is equally applicable to clinical dyspneas in which this or another reflex drive comes into play. There is some evidence that the rapid, shallow breathing of severe, prolonged anoxemia is due to a direct effect of anoxia on the brain itself, and this is indicated under "Impulses from Cortex." The most striking change in viewpoint is seen in the dyspnea of exercise, for this, according to evidence now available[2], appears to be due mainly to afferent impulses from the exercising muscles (included under "Elsewhere" in the table) and to the rise in body temperature associated with increased muscular activity; irradiation of impulses from the cortex into the center has been suggested as an additional factor, but increase in the action of chemical stimuli on the center is now known not to be essential. Since the hyperpnea of exercise is both the commonest and the most powerful of all respiratory adjustments, one may derive from these findings an added respect for the importance of reflex factors in respiratory control.

This same preponderance of reflex over direct chemical stimulation is seen in the dyspneas encountered in disease, for none of these now seems to be due entirely to influences of the latter type. The dyspnea of heart disease, as Christie[1] has already pointed out, depends more on reflexes from the lungs than on any other single factor, but if anoxemia is present the chemoreceptors will be stimulated; anxiety will contribute impulses from the cortex and the high venous pressure may so interfere with the circulation through the respiratory center as to cause accumulation there of products of its own metabolism[5], p. 655. In pneumonia stimulant reflexes from the lungs are probably aroused by irritation of the air passages, pain from the inflamed pleural surfaces can stimulate breathing reflexly, anoxemia sets up chemoreceptor reflexes, and fever may also stimulate either directly or reflexly. In atelectasis, whether due to bronchial obstruction or pneumothorax, stimulant reflexes are originated in the lungs by collapse of parts of the alveolar system, anoxemia is present to stimulate the carotid and aortic bodies, and a certain amount of CO_2 retention may also take place[6]. In emphysema pulmonary fibrosis is apt to occur and this, as well as the reduction in alveolar area, will lead to anoxemia and CO_2 retention. In asthma reflexes may be set up in the lungs by the fluid in the air passages; some anoxemia as well as some CO_2 retention may also be present. The dyspnea of anemia has no adequate explanation at the moment; perhaps acid products of metabolism accumulate in the respiratory center or elsewhere and stimulate breathing directly or reflexly; perhaps carbonic anhydrase, which is present only in the erythrocytes, is so lacking as to permit arterial CO_2 tension to rise, particularly on exertion. In shock, hemorrhage or other rapidly induced hypotension terminal dyspnea may occur and this, as far as is now known, is due to inactivation (by the hypotension) of inhibitory reflexes from the carotid and aortic pressoreceptors, to excitement and apprehension, and to reduction in the blood supply of the center. Finally, during the inhalation of ether pulmonary ventilation is typically at or above the normal level even during the stage of complete surgical anesthesia; this is not because ether does not depress the respiratory center, but because it gives rise to stimulant reflexes in the lungs and in the limbs[4], and the central depression is overcome by these.

One of the outstanding features in clinical dyspneas is their tendency to exaggeration by exertion. The reason for this, like that for the dyspnea itself, now seems to vary according to the condition and not to be subject to any single, all-inclusive explanation. Space does not permit, nor does existing evidence justify, a detailed consideration of this subject at this time. As pointed out elsewhere[5], the various factors involved in dyspnea show a noteworthy tendency toward summation; from what is now known about the factors responsible for the hyperpnea of exercise it is obvious that these factors, coming into play in a system in which other reflex factors are already operating to stimulate breathing, will produce further breathlessness which the increased pulmonary ventilation cannot alleviate. Exertion implies increased consumption of oxygen and increased production of CO_2, and any preexisting tendency to anoxemia or CO_2 retention would thus be exaggerated.

From this brief discussion it should be evident that much remains to be learned about the cause of dyspnea. The situation is probably much more complex than we have pictured it. The important questions can be answered only by careful clinical studies, which we hope will soon be made.

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